

REMARKS

I. Status of the Claims

Upon entry of the present amendment, claims 1-30 are pending in this application. Applicant note that claim 9 is drawn to the elected species of group A wherein the biopolymer is an oligosaccharide, of which agarose is a member and group D wherein the support is glass. The withdrawal of claim 9 is therefore improper and Applicants respectfully request that this claim be rejoined. Claims 11-13 are currently amended; claims 10 and 14-28 are withdrawn from consideration and claims 29 and 30 are new. The amendment to claims 11-13 are made to maintain proper antecedent basis. New claim 29 is more specifically directed to a microarray of preformed ligand-modified biopolymer and new claim 30 is directed to a microarray of claim 1 made by the method of 14. No new matter is introduced.

II. Claim Rejections

A. 35 U.S.C. §112, Second Paragraph

Claims 1-8 and 11-13 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Specifically, the Patent Office asserts that it is unclear whether the spotted biopolymers are intended to form a plurality of discrete regions or whether discrete regions exist on the substrate and the substrate further comprises a spotted biopolymer. Further the Patent Office asserts that it is unclear whether the phrase "can be the same or different" refers to ligands in any of the discrete regions or whether the ligand in the discrete regions can merely be capable of being the same or different. Applicants respectfully traverse these rejections.

To satisfy the statutory requirement under 35 U.S.C. §112, second paragraph, claims must particularly point out and distinctly claim the subject matter of the invention. MPEP §2173. The essential inquiry pertaining to the definiteness requirement is whether a claim sets out and circumscribes a particular subject matter with a reasonable degree of clarity and particularity so as to appraise one of skill in the art of the claim scope. An indefiniteness rejection is not appropriate when a person of ordinary skill in the art could interpret the metes and bounds of the claim. MPEP §2173.02. The definiteness of a claim must be considered as a whole and in light of:

(A) The content of the particular application disclosure;
(B) The teachings of the prior art; and
(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP §2173.02.

Applicants contend that the specification provides a definition of the microarray which complies with the threshold requirement for clarity and precision. For example at paragraph 27 the specification states:

The terms "array" and "microarray" are used interchangeably, and are each intended to include a solid support having a suitable ligand immobilized on at least one spatially distinct region of its surface. An array can contain any number of ligands immobilized within any number of spatially distinct regions. The spacing and orientation of the ligands can be regular, e.g., in a rectangular or hexagonal grid, or the pattern can be irregular or random. In a particular embodiment, non-identical ligands are arranged in a regular pattern on the surface of a solid support and are useful, for example, in binding assays to determine whether analytes (capable of binding to selected ligands) are present in a sample. Ligands capable of detecting the presence of a component can be placed in a spatially distinct region, so that in a single analysis, a determination can be made as to whether one or more of the components of the set are contained within the sample.

While this example does not serve to limit the scope of the claims, Applicants contend that there is no ambiguity that the specification provides that spotting of the biopolymers defines the plurality of discrete regions and that the microarray can encompass the same or different ligands in any of these discrete regions. Because the specification allows one of skill in the art to determine the metes and bounds of the claimed invention, the withdrawal of these indefiniteness rejections are respectfully requested.

Finally, the Patent Office asserts insufficient antecedent basis for the recitation "the difference in concentration" in claims 11-13. As amended, claims 11-13 now recites "the concentration in said discrete regions varies" and therefore, the indefiniteness rejection is obviated. As such, Applicants submit that the indefiniteness rejection should be properly withdrawn.

B. Under 35 U.S.C. §102(b)

Claims 1-3 and 7 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Li, U.S. Patent No. 6,704,104 (hereinafter "Li"); and claims 1 and 4-6 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Chenchik, U.S. Patent No. 6,489,159 (hereinafter "Chenchik"). Applicants respond in part by amendment and in part traverse the rejection.

To anticipate a pending claim, a prior art reference must provide all limitations of the claim. MPEP §2131, citing *Richardson v. Suzuki*, 868 F.2d 1226 (Fed. Cir. 1991). Independent claim 1 is drawn to a microarray comprising a support having a plurality of discrete regions having a biopolymer spotted thereon, wherein attached to said biopolymer in each of said regions is a ligand that can be the same or different from a ligand in any other of said discrete regions, and wherein the concentration of said ligand in said discrete regions is substantially normalized; (emphasis added). Applicants submit that this element of the claims now pending has not been disclosed in the references cited above. Therefore, Applicants respectfully traverse the rejection.

The Patent Office alleges that Li discloses an array wherein the amount of light which corresponds to the concentration of the ligand is normalized and that this embraces the Applicants' instantly claimed array wherein the concentration of the ligand on the substrate is substantially normalized. The Patent Office points to the description of Figures 9a and 9b of Li which show the image dispersion after collecting and normalizing the fluorescence signals from the array. Applicants note that this normalization procedure of Li is to obviate the need to correct for any skew among the received pixels in the sensed image during subsequent processing. Li at Col. 13 lines 39 to 48. While Li discloses normalized fluorescence signals, Li does not disclose arrays wherein the ligand concentration is normalized as required by the claims. Because the arrays disclosed do not normalize ligand concentration on the substrate, Li does not anticipate the microarrays of claim 1 under 35 U.S.C. §102(b).

In addition, the Patent Office alleges that Chenchik also disclose an array on a substrate wherein the concentration of the ligand is normalized. The Patent Office points to the description in Col. 13, lines 4-30 which recites:

In certain embodiments, the above described methods further include use of a normalization protocol. This particular normalization protocol provides a method for normalizing relative amounts of target compositions, e.g., samples (such as nucleic acids derived from an RNA sample, as described above), by employing an integral factor that is determined based on a set of internal reference ribonucleic acids. The reference ribonucleic acids, e.g., housekeeping genes, used to generate the integral factor are preferably expressed in all cells with medium to high relative abundance and possess low or moderate tissue to tissue variability. Once determined, the integral factor allows a relative determination of integral or total transcript levels in a sample based on the levels of one or more of the reference ribonucleic acids in the sample. Based on the measured expression level of test mRNA, the level of any reference mRNA, and the integral factor, the procedure allows one to normalize the expression level of test mRNAs between multiple samples. This procedure allows the determination of the relative level of a test transcript between samples without being dependent of the actual levels of total RNA assayed, thus obviating the requirement for normalization of total mRNA amount prior to loading multiple samples onto an array. Preferably, the selected reference nucleic acids are housekeeping gene products (or transcripts), and more preferably the reference nucleic acids of a selected set belong to different functional classes of genes.

Applicants note that this normalization procedure of Chenchik is to obviate the need to normalize ligand concentration. Therefore, Chenchik specifically discloses that the ligand concentration is not normalized as required by the claims. As such, even if one were to follow the procedures of Chenchik one would not obtain the arrays of the presently claimed invention. Because the arrays disclosed do not normalize ligand concentration on the substrate, Chenchik does not anticipate the microarrays of claim 1 under 35 U.S.C. §102(b).

Applicants submit, therefore, that claim 1 is not anticipated by any of the cited references under 35 U.S.C. §102(b). Because the cited references do not anticipate independent claim 1, these references do not anticipate claims which depend therefrom.

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Accordingly, Applicants submit that the cited references fail to anticipate the present invention and respectfully request that this rejection under 35 U.S.C. §102(b) be withdrawn.

C. Under 35 U.S.C. §103(a)

Claims 8 is rejected under 35 U.S.C. §103(a) as allegedly being obvious over Li, in view of Bertozzi, U.S. Patent Application No. 2003/0073157 (hereinafter " Bertozzi "); and claims 11-13 were rejected under 35 U.S.C. §103(a) for allegedly being obvious over Chenchik *et al.*. Applicants traverse the rejection.

To render obvious a pending claim, a prior art reference must provide all limitations of the claim. MPEP §2143:

[t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the prior art reference (or references when combined) *must teach or suggest all the claim limitations*. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure.

As set forth herein, the alleged prior art references do not teach or suggest all the claim limitations and thus, a *prima facie* case of obviousness of the claims has not been established

Dependent claim 8 is drawn to a microarray comprising a support having a plurality of discrete regions having a biopolymer spotted thereon, wherein attached to said biopolymer in each of said regions is a ligand that can be the same or different from a ligand in any other of said discrete regions, and wherein the concentration of said ligand in said discrete regions is substantially normalized; and wherein said ligand is attached to said biopolymer via chemoselective ligation (emphasis added). Dependent claims 11-13 are drawn to a microarray comprising a support having a plurality of discrete regions having a biopolymer spotted thereon, wherein attached to said biopolymer in each of said regions is a ligand that can be the same or

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different from a ligand in any other of said discrete regions, and wherein the concentration of said ligand in said discrete regions is substantially normalized; and wherein the concentration between any two discrete regions varies less than a certain percentage.

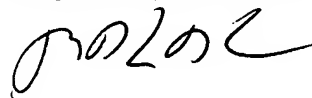
As set forth above, Li and Chenchik *et al.* do not disclose, teach or suggest an array wherein ligand concentration is substantially normalized. Bertozzi does not cure the deficiencies of these references. Bertozzi does not even mention normalization and therefore cannot teach or suggest that the ligand concentration is normalized or within a particular range. Applicants submit that the limited teaching of Bertozzi would also fail to motivate one skilled in the art to prepare any arrays in which ligand concentration is normalized. In the absence of any direction in Bertozzi, Applicants submit that the cited references do not teach or suggest the claimed features of the present invention and respectfully request that the present rejection be withdrawn and send this application to issue.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Patent Office believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5014.

Respectfully submitted,



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